Dexamethasone and cyclosporin A modulation of human retinal pigment epithelial cell monocyte chemotactic protein-1 and interleukin-8.

Kurtz RM, Elner VM, Bian ZM, Strieter RM, Kunkel SL, Elner SG

Department of Ophthalmology (Kellogg Eye Center), University of Michigan, Ann Arbor 48105, USA.

PURPOSE: To examine the modulation of interleukin-1 beta (IL-1 beta)- and tumor necrosis factor-alpha (TNF-alpha)-stimulated monocyte chemotactic protein-1 (MCP-1) and interleukin-8 (IL-8) secretion and transcription in human retinal pigment epithelial (HRPE) cells by dexamethasone (DEX) and cyclosporin A (CSA). METHODS: Cultured HRPE cells were stimulated with IL-1 beta (0.2 to 20 ng/ml) or TNF-alpha (0.2 to 20 ng/ml) for 8 or 24 hours without (control) and with DEX (10(-8) to 10(-6) M) or with CSA (0.3 to 30 ng/ml). Secreted levels of HRPE MCP-1 and IL-8 were measured in the media using enzyme-linked immunosorbent assay (ELISA). Both MCP-1 and IL-8 mRNA were analyzed by Northern blot. RESULTS: Although DEX (10(-8) to 10(-6) M) inhibited IL-1 beta-stimulated MCP-1 and IL-8 production, it did not inhibit TNF-alpha-stimulated chemokine secretion. In contrast, CSA significantly inhibited TNF-alpha-stimulated, but not IL-1 beta-stimulated, HRPE MCP-1 and IL-8 secretion. Both DEX and CSA inhibitions showed dose dependence. Northern blot analysis of HRPE steady state MCP-1 and IL-8 mRNA corroborated the ELISA measurements of secreted MCP-1 and IL-8. CONCLUSIONS: Although DEX and CSA inhibit HRPE MCP-1 and IL-8 secretion, this is dependent on whether the inducing inflammatory mediator is IL-1 beta or TNF-alpha. IL-1 beta-induced chemokine secretion is sensitive to DEX, whereas MCP-1 and IL-8 induced by TNF-alpha are inhibited by CSA. This information may be useful in explaining in vivo observations and in suggesting targeted clinical treatments and combinations of immunosuppressive agents.

PMID: 9040477, UI: 97192885

JMurphy3_Job_1_of_1

Printed by HPS Server

for

EAST

Printer: cm1_9e12_gbefptr

Date: 02/08/00

Time: 15:37:18

Document Listing

Document	Selected Pages	Page Range
US005936068	27	1 - 27
US005665346	28	1 - 28
US005656724	40	1 - 40
US005591718	24	1 - 24
US005556757	49	1 - 49
US005510264	50	1 - 50
US005413778	8	1 - 8
Total (7)	226	-